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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/573,972

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EXAMINER

ROBINSON, BINTA M

ART UNIT

PAPER NUMBER

1625

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/573,972	<b>Applicant(s)</b> TAKADA ET AL.	
	<b>Examiner</b> BINTA M. ROBINSON	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____.                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/13/2006</u> .   | 6) <input type="checkbox"/> Other: ____.                          |

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### Detailed Action

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this

Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Sakoda et. al.. Sakoda et. al. teaches the instant process of obtaining the compound of formula 6 which reads on the instant final product, by recrystallizations of the compound of formula 6 to 100% enantiomeric purity from ethanol. See page 9, lines 3-5, and the right column. This prior art process anticipates the process wherein a mixture of the compound of formula 1 in which either one of the optically active compounds thereof is present in excess in a solvent to prepare a supersaturated solution; and adding a crystal of the one optically active substance present in excess as a seed crystal in the supersaturated solution to allow the crystal of the one optically active substance present in excess to separate out. Recrystallization by definition typically involves a scenario where the mixture of "compound A" and "impurity B" are dissolved in the minimum amount of solvent to fully dissolve the mixture i.e. a supersaturated solution. The solution is then allowed to cool. As the solution cools the solubility of compounds in solution drops. This results in the desired compound dropping (recrystallizing) from solution. The slower the rate of cooling, the bigger the crystals formed.

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In terms of seeding, the crystallization process requires an initiation step. Once a small crystal has formed, more crystals can grow from that crystal. Since "Compound A" is in excess, this will usually result in these crystals forming first and thus leaves a greater ratio of impurity in solution. Thus the resulting solid is more pure than the original mixture.

The term "recrystallization" in the prior art encompasses applicant's instant steps.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsumoto et. al... Matsumoto et. al. teaches the instant process of obtaining the compound of formula 1 which reads on the instant final product, by recrystallizing the compound of formula 1 and improving the optical purity by this recrystallization of compounds of formula I of the (R ) enantiomer by means of recrystallization in ethyl acetate or ethanol. See the second upper right column of page 5 and see compound 1 on page 2. This prior art process anticipates the process wherein a mixture of the compound of formula 1 in which either one of optically active compounds thereof is present in excess in a solvent to prepare a supersaturated solution; and adding crystal of the one optically active substance present in excess as a seed crystal in the supersaturated solution to allow one of the crystals of the one optically active substance present in excess to separate out. Recrystallization by definition typically involves a scenario where the mixture of "compound A" and "impurity B" are dissolved in the minimum amount of solvent to fully dissolve the mixture i.e. a supersaturated solution. The solution is then allowed to cool. As the solution cools the solubility of compounds in solution drops. This

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In terms of seeding, the crystallization process requires an initiation step. Once a small crystal has formed, more crystals can grow from that crystal. Since "Compound A" is in excess this will usually result in these crystals forming first and thus leaves a greater ratio of impurity in solution. Thus the resulting solid is more pure than the original mixture. The term "recrystallization" in the prior art encompasses applicant's instant steps.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakoda et. al. as applied to claims 1-4 above, and further in view of Brittain et. al.

Sakoda et. al. teaches the process of obtaining the compound of formula 6 which reads on the instant final product, by recrystallizations of the compound of formula 6 to 100% enantiomeric purity from ethanol. See page 9, lines 3-5, the right column. The difference between the prior art process and the instantly claimed process is the that the prior art process involves dissolving a mixture of the compound of formula (1) in which one of the optically enantiomers is enriched in the solution and recrystallized from it versus the instant process which

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alternatively teaches a process consisting of dissolving a racemate of the compound of formula (1) in a solvent to prepare a supersaturated solution; and adding a crystal of either one of the optically active compounds of formula (1) as a seed crystal in the supersaturated solution to allow a crystal of one of the optically active compounds added as the seed crystal to separate out. Brittain teaches that the instantly claimed process not taught in the prior art, is a conventional method of separating enantiomers from racemic mixtures. Brittain teaches that enantiomorphic crystals can be separated while formed simultaneously in a mother liquor which remains racemic. Seed crystals are obtained and are required for the direct crystallization to produce larger quantities of the resolved material. See page 687 of Brittain, second column. Brittain also teaches that when a compound forms a true racemate, that this compound can be formed via a derivatization reaction, wherein resolving agents are used to form dissociable diastereomer species, wherein fractional crystallization is further used to purify the enantiomers. See the first and second columns of page 688 of Brittain under the section "Resolution of True Racemates". It would have been obvious to one of ordinary skill in the art to use conventional methods of resolution of racemates to produce the final instant product. Accordingly, the instant process is deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed process over those of the prior art process.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matsumoto et. al. as applied to claims 1-4 above, and further in view of Brittain et. al.

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Matsumoto et. al. teaches the instant process of obtaining the compound of formula 1 which reads on the instant final product, by recrystallizing the compound of formula 1 and improving the optical purity by this recrystallization of compounds of formula I of the (R ) enantiomer by means of recrystallization in ethyl acetate or ethanol. See the second upper right column of page 5 and see compound 1 on page 2. The difference between the prior art process and the instantly claimed process is that the prior art process involves dissolving a mixture of the compound of formula (1) in which one of the optically enantiomers is enriched in the solution and recrystallized from it versus the instant process which alternatively teaches a process consisting of dissolving a racemate of the compound of formula (1) in a solvent to prepare a supersaturated solution; and adding a crystal of either one of the optically active compounds of formula (1) as a seed crystal in the supersaturated solution to allow a crystal of one of the optically active compounds added as the seed crystal to separate out. Brittain teaches that the instantly claimed process not taught in the prior art, is a conventional method of separating enantiomers from racemic mixtures. Brittain teaches that enantiomorphic crystals can be separated while formed simultaneously in a mother liquor remains which racemic. Seed crystals are obtained and are required for the direct crystallization to produce larger quantities of the resolved material. See page 687 of Brittain, second column. Brittain also teaches that when a compound forms a true racemate, that this compound can be formed via a derivatization reaction, wherein resolving agents are used to form dissociable diastereomer species, wherein fractional crystallization is further

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used to purify the enantiomers. See the first and second columns of page 688 of Brittain under the section "Resolution of True Racemates". It would have been obvious to one of ordinary skill in the art to use conventional methods of resolution of racemates to produce the final instant product. Accordingly, the instant process is deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed process over those of the prior art process.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sakoda et. al. as applied to claims 1-4, and further in view of Brittain et. al. and Gogassy et. al. (Hcaplus 144:22428).

Sakoda et. al. teaches the process of obtaining the compound of formula 6 which reads on the instant final product, by recrystallizing the compound of formula 6 in 100% enantiomeric purity from ethanol. See page 9, lines 3-5, the right column. The difference between the prior art process and the instantly claimed process is the teaching of ethanol rather than an aromatic hydrocarbon of the formula 2 as the recrystallization solvent and resolution agent. Gogassy et. al. (Hcaplus 144:22428) teaches that some examples exist where a racemic compound could be favorably be resolved with resolution agents having related structures. Here, an aromatic hydrocarbon of the formula 2 has shares a similar

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structure to the racemic compound with regard to the phenyl rings. There are three phenyl rings in the racemic mixture. Additionally, Brittain teaches that enantiomer separation can occur when a solution is prepared which contains a slight excess of one enantiomer. Crystallization is induced (usually with the aid of appropriate seed crystals), whereupon the desired enantiomer is obtained as a solid and the mother liqueur is enriched in the other isomer. See page 687, second column of Brittain. In Brittain, the solution in which the excess of one enantiomer is obtained is not specified, and could conceivably include an aromatic hydrocarbon of formula 2. It would have been obvious to one of ordinary skill in the modify the prior art process to substitute an aromatic hydrocarbon of formula 2 for ethanol as the resolution agent and recrystallization solvent in the process of producing the compound of formula I. Accordingly, the process is deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed process over those of the generic prior art process.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Matsumoto et. al.

Matsumoto et. al. teaches the process of obtaining the compound of formula 1 which reads on the instant final product, by recrystallizing the compound of formula 1 and improving the optical purity by this recrystallization of compounds of formula I of the (R ) enantiomer by means of recrystallization in ethyl acetate or ethanol. See the second upper right column of page 5 and see compound 1 on page 2.

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The difference between the prior art process and the instantly claimed process is the teaching of ethanol or ethyl acetate rather than an aromatic hydrocarbon of the formula 2 as the recrystallization solvent and resolution agent. Gogassy et. al. (Hcaplus 144:22428) teaches that some examples exist where a racemic compound could be favorably be resolved with resolution agents having related structures. Here, an aromatic hydrocarbon of the formula 2 shares a similar structure to the racemic compound with regard to the phenyl rings. There are three phenyl rings in the racemic mixture. Additionally, Brittain teaches that enantiomer separation can occur when a solution is prepared which contains a slight excess of one enantiomer. Crystallization is induced (usually with the aid of appropriate seed crystals), whereupon the desired enantiomer is obtained as a solid and the mother liqueur is enriched in the other isomer. See page 687, second column of Brittain. In Brittain, the solution in which the excess of one enantiomer is obtained is not specified, and could conceivably include an aromatic hydrocarbon of formula 2. It would have been obvious to one of ordinary skill in the modify the prior art process to substitute an aromatic hydrocarbon of formula 2 for ethanol as the resolution agent and recrystallization solvent in the process of producing the compound of formula I. Accordingly, the process is deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed process over those of the generic prior art process.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

/JANET L ANDRES/  
Supervisory Patent Examiner, Art Unit 1625

BMR  
July 22, 2008